



Economic Evaluation of Screening for Hereditary Hemochromatosis

Scott Grosse, PhD

**Public Health Assessment of Genetic Tests for
Screening and Prevention**

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Economic Evaluation in Healthcare and Public Health

- **Quantitative assessment of expected benefits and costs**
 - Identify relevant health outcomes
 - Attach probabilities to outcomes
 - Attach values and costs to outcomes
 - Sum up
- **Dueling purposes**
 - Objective decision-making
 - Advocacy



Framing an Economic Evaluation

- Choose a policy-relevant question
 - Be specific in describing interventions
 - Consider all relevant alternatives
- Identify audience and perspective
 - Health care system
 - Public health & society
- Include all costs relevant to perspective
- Specify assumptions about health outcomes
 - Include probabilities, not just point estimates
- Address time frame and discounting

Economic Evaluation: Cost-Effectiveness Analysis

- **Purpose: Determine least expensive way to achieve outcome**
- **Partial CEA – outcome of cases detected**
 - Assumes earlier detection has benefits
 - Excludes treatment costs
 - Excludes averted costs of care
- **Full CEA – health outcomes**
 - Calculate net monetary costs and health outcomes for each strategy
 - If one strategy costs less and has better outcomes, it “dominates” other strategies and is “cost saving”
 - If one strategy is both more effective and costs more, calculate cost-effectiveness ratio



Calculating Costs

- Use resource costs, not charges
- Intervention costs
 - All costs, not just costs paid by program
 - Cost components
 - ◆ Education and counseling prior to screening
 - ◆ Diagnosis and genetic counseling
 - ◆ Treatment and monitoring
 - ◆ Patient time costs (for societal perspective)
- Disease costs
 - Healthcare costs with and without program
- Discount future year costs to present value (3% per year in U.S., 6% in U.K.)



Calculating Health Outcomes

- Deaths averted or life years gained
- Quality-adjusted life years (QALYs)
 - Metric for both morbidity and mortality
 - Multiply time spent in each health state by health state utility (1=health, 0=death)
- Discount future year outcomes to present value (varies by country)
- Cost-effectiveness analyses recommended to use QALYs (cost-utility analysis), but
 - Whose preferences?
 - How to measure preferences?

Interpretation of Cost-Effectiveness Ratios

- Usual approaches
 - Decision rule
 - ◆ If CER > \$50,000 per QALY (or LY), cost-effective
 - ◆ If CER > \$100,000 per QALY, not cost-effective
 - League table
 - ◆ Compare CER with accepted programs, e.g., mammography
 - Limitations
- Policy makers must decide acceptable value
 - May vary according to type of intervention
 - May differ for deaths and illness
 - Likely to differ among payers



Addressing Uncertainty

- Establish range of plausible values for each model parameter
- Sensitivity and threshold analyses
- Purposes
 - Determine robustness of conclusion
 - Identify influential parameters
 - Help set priorities for data collection



Issues to Consider in Assessing CEAs

- Who are the analysts? Any bias?
- Was relevant policy question addressed?
- Were appropriate alternatives included?
- Was perspective stated? Correctly followed?
- Were important costs excluded?
- Are cost estimates credible?
- Are assumptions of effectiveness conservative?
Evidence-based?
- Did sensitivity analysis vary multiple parameters?
- Are conclusions appropriate? Caveats?

Hereditary Hemochromatosis (HH): Challenges for Mass Screening

- **Clinical validity**
 - Pentrance of genotypes
 - Expression of phenotypes
- **Clinical utility**
 - Natural history without screening
- **Ethical, legal, and social issues**
 - Insurance discrimination
 - Use of transfused blood
 - Unnecessary treatment

Cost-Effectiveness Analyses of Hemochromatosis Screening

- **Published CEAs (see list)**
 - 7 studies published 1994-1997 reviewed by Grosse & Teutsch (2000)
 - 7 more recent studies 1999-2002
 - All conclude screening for HH is cost-effective
 - All 14 prepared by advocates of screening
- **Types of screening evaluated**
 - **Phenotypic screening**
 - ◆ Adult men
 - ◆ Hospital patients
 - ◆ Blood donors
 - ◆ Employees
 - **Genetic (DNA) screening**
 - ◆ Cascade screening of relatives
 - ◆ Blood donors



Common Pitfalls in HH CEAs

- No clear policy question
 - How will screening be offered and to whom?
 - Will people be screened only once?
- Optimistic assumptions favorable to screening
 - Prevalence
 - Penetrance or expression
 - Uptake of screening
 - Compliance with treatment
- Problems with costs
 - Test costs often understated
 - Counseling and other costs excluded
 - Patient costs excluded
- Ignore other conditions identified (e.g. ID anemia)
- Limited sensitivity analyses



Partial CEA of HH Screening in U.S. (Stave et al. 1999)

■ Protocol

- Screen employees having blood drawn for other reasons for iron/transferrin
- Those with elevated TS and elevated ferritin referred for liver biopsy

■ Assumptions

- Epidemiology
 - ◆ Of 1968 employees screened, 16 screened positive
 - ◆ Of 16 referred, 3 received liver biopsy, all diagnosed with HH
 - ◆ Assumed gain in life years per case diagnosed: 10
- Cost
 - ◆ Liver biopsy and examination \$1500
 - ◆ Maintenance cost: not considered

■ Results

- Cost of screening \$27,850 (1968 blood tests and 3 liver biopsies)
- Cost of screening \$14.15 per person
- Life years gained: 15.2 per 1000 persons screened
- Cost-effectiveness ratio: \$928 per life year gained



Full CEA of HFE Screening in Germany (Schoffski et al. 2000)

- **Protocol**
 - Screen 25-year-old males for C282Y alleles
 - Homozygotes offered phlebotomy Tx
- **Assumptions**
 - Epidemiology
 - ◆ Prevalence 2.5 per 1000
 - ◆ Analytic sensitivity 100%
 - ◆ Clinical Sensitivity 90%
 - ◆ Specificity 100%
 - ◆ Penetrance 10%
 - ◆ Life-reducing complication 43%
 - Cost
 - ◆ DNA test 5 EUR
 - ◆ Maintenance cost 50 EUR per year
- **Results**
 - Cost of screening 7.26 EUR per person screened
 - Net cost of screening 5.62 EUR per person
 - Life years gained: 1.3 per 1000 persons screened
 - Cost-effectiveness ratio: 4,461 EUR per life year gained



Partial CEA of TS Screening in Norway (Asberg et al. 2002)

■ Protocol

- Screen 30-year-old males for elevated non-fasting transferrin saturation
- Repeat fasting TS, followed by serum ferritin, confirm by HFE test

■ Assumptions

– Epidemiology

- ◆ Prevalence 7 per 1000
- ◆ Sensitivity of screening 89%
- ◆ Sensitivity of genotyping 100%
- ◆ Specificity for first screen 97.8%
- ◆ Probability of liver cirrhosis 15%

– Cost

- ◆ First screening test \$0.32 (reagents only) or \$9.73 (charge)
- ◆ DNA test and clinical exam \$167.76
- ◆ Maintenance cost: none assumed

■ Results

- Cost of screening \$1.91 or \$11.32 per person screened
- Life years gained: 7.3 per 1000 persons screened
- Cost-effectiveness ratio: \$263 or \$1559 per life year gained



Conclusions

- Is population screening for HH cost-effective?
 - Plausible but not proven
 - Better outcomes data needed
 - Realistic screening scenarios needed
 - Objective, rigorous CEA needed, once effectiveness data are available
- How to read published CEAs
 - Be skeptical – caveat lector!
 - Apply criteria for good CEAs
 - Epidemiology is often the weak link
 - Demand evidence of effectiveness

